Form PTO-1449

INFORMATION DISCLOSURE CITATION IN AN APPLICATION

(Use several sheets if necessary)

Docket Number 300622000212	Application Number 09/870,012
Applicant: Chaitan KHOSLA et al. #3	
Filing Date May 29, 2001	Group Art Unit 1652
Mailing Date February 20, 2002	

U.S. PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Filing Date If Appropriate
KK	1.	10/1998	5,824,513	Katz			
↓	2.	12/1995	5,475,099	Knauf *et al.*			

FOREIGN PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Country	Class	Subclass	Translation YES	Translation NO
KK	3.	4/1997	WO 97/13845	WIPO				
	4.	1/1997	WO 97/02358	WIPO				
	5.	3/1995	WO 95/08548	WIPO				
↓	6.	7/1993	WO 93/13663	WIPO				

OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
KK	7.	Aparicio *et al.*, "Limited Proteolysis and Active-Site Studies of the First Multienzyme Component of the Erythromycin-Producing Polyketide Synthase," J BIOL CHEM (1994) 269(11):8524-8528
	8.	Bartel *et al.*, "Biosynthesis of Anthraquinones by Interspecies Cloning of Actinorhodin Biosynthesis Genes in Streptomycetes: Clarification of Actinorhodin Gene Functions," J BACTERIOL (1990) 172(9):4816-4826
	9.	Beck *et al.*, "The Multifunctional 6-Methylsalicylic Acid Synthase Gene of *Penicillium Patulum*. Its Gene Structure Relative to that of Other Polyketide Synthases," EUR J BIOCHEM (1990) 192:487-498
	10.	Bedford *et al.*, "A Functional Chimeric Modular Polyketide Synthase Generated via Domain Replacement," CHEMISTRY & BIOLOGY (1996) 3(10):827-831
	11.	Bevitt *et al.*, "6-Deoxyerythronolide-B Synthase 2 from *Saccharopolyspora erythraea:* Cloning of the Structural Gene, Sequence Analysis and Inferred Domain Structure of the Multifunctional Enzyme," EUR J BIOCHEM (1992) 204:39-49
	12.	Bibb *et al.*, "Analysis of the Nucleotide Sequence of the *Streptomyces Glaucescens tcml* Genes Provides Key Information about the Enzymology of Polyketide Antibiotic Biosynthesis," EMBO J (1989) 8(9):2727-2736
↓	13.	Caballero *et al.*, "Organisation and Functions of the *act*VA Region of the Actinorhodin Biosynthetic Gene Cluster of *Streptomyces coelicolor*," MOL GEN GENET (1991) 230:401-412

EXAMINER: Kathleen Kerr — DATE CONSIDERED: 11/20/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449	Docket Number 300622000212	Application Number 09/870,012
INFORMATION DISCLOSURE CITATION IN AN APPLICATION	Applicant: Chaitan KHOSLA et al.	
	Filing Date May 29, 2001	Group Art Unit 1652
(Use several sheets if necessary)	Mailing Date February 20 2002	

OTHER DOCUMENTS *(including author, title, Date, Pertinent Pages, Etc.)*

Examiner Initials	Ref. No.	Title
KK	14.	Caffrey *et al.*, "An Acyl-Carrier-Protein-Thioesterase Domain from the 6-Deoxyerythronolide B Synthase of *Saccharopolyspora erythraea.* High-Level Production, Purification and Characterisation in *Escherichia coli*," EUR J BIOCHEM (1991) 195:823-830
	15.	Caffrey *et al.*, "Identification of DEBS 1, DEBS 2 and DEBS 3, the Multienzyme Polypeptides of the Erythromycin-Producing Polyketide Synthase from *Saccharopolyspora erythraea*," FEBS LETT (1992) 304(2):225-228
	16.	Cane *et al.*, "Macrolide Biosynthesis. 7. Incorporation of Polyketide Chain Elongation Intermediates into Methymycin," J AM CHEM SOC (1993) 115:522-526
	17.	Corcoran *et al.*, "The Biogenesis of Fatty Acids and Erythronolide-Like Substances in Mycelium-Free Extracts of *Streptomyces Erythreus*," in 5th International Congress of Chemotherapy, Vienna, ABSTRACTS OF COMMUNICATIONS (1967) 35-40
	18.	Corcoran, ed., in Antibiotics Volume IV Biosynthesis, Springer-Verlag, New York (1982) 145-150
	19.	Cortes *et al.*, "An Unusually Large Multifunctional Polypeptide in the Erythromycin-Producing Polyketide Synthase of *Saccharopolyspora erythraea*," NATURE (1990) 348:176-178
	20.	Daum *et al.*, "Mutational Biosynthesis of New Antibiotics," ANN REV MICROBIOL (1979) 33:241-265
	21.	Davis *et al.*, "Functional Mapping of a Polyketide Synthase from *aspergillus terreus* Involved in Lovastatin Synthesis," Abst. of the Genetics of Industrial Microorganisms Mtg. (1994) 288:192
	22.	Dimroth *et al.*, "Biosynthese Von 6-Methylsalicylsaure," EUR J BIOCHEM (1970) 13:98-110
	23.	Donadio *et al.*, "Modular Organization of Genes Required for Complex Polyketide Biosynthesis," SCIENCE (1991) 252:675-679
	24.	Donadio *et al.*, "Organization of the Enzymatic Domains in the Multifunctional Polyketide Synthase Involved in Erythromycin Formation in *Saccharopolyspora erythraea*," GENE (1992) 111:51-60
	25.	Donadio *et al.*, "Biosynthesis of the Erythromycin Macrolactone and a Rational Approach for Producing Hybrid Macrolides," GENE (1992) 115:97-103
	26.	Donadio *et al.*, "An Erythromycin Analog Produced by Reprogramming of Polyketide Synthesis," PROC NATL ACAD SCI USA (1993) 90:7119-7123
	27.	Dutton *et al.*, "Avermectin Biosynthesis. Intact Incorporation of a Diketide Chain-Assembly Intermediate into the Polyketide Macrocycle Ring," TETRAHEDRON LETTERS (1994) 35(2):327-330
	28.	Dutton *et al.*, "Novel Avermectins Produced by Mutational Biosynthesis," J ANTIBIOT (1991) 44(3):357-365
V	29.	Fernandez-Moreno *et al.*, "The *act* Cluster Contains Regulatory and Antibiotic Export Genes, Direct

EXAMINER: [signature] DATE CONSIDERED: 11/20/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION	Docket Number 300622000212	Application Number 09/870,012
	Applicant: Chaitan KHOSLA et al.	
	Filing Date May 29, 2001	Group Art Unit 1652
(Use several sheets if necessary)	Mailing Date February 20, 2002	

OTHER DOCUMENTS *(including author, title, Date, Pertinent Pages, Etc.)*

Examiner Initials	Ref. No.	Title
		Targets for Translational Control by the *bldA* tRNA Gene of Streptomyces," CELL (1991) 66:769-780
KK	30.	Fernandez-Moreno *et al.*, "Nucleotide Sequence and Deduced Functions of a Set of Cotranscribed Genes of *Streptomyces coelicolor* A3(2) Including the Polyketide Synthase for the Antibiotic Actinorhodin," J BIOL CHEM (1992) 267:19278-19290
	31.	Gokhale et al., "Functional Orientation of the Acyltransferase Domain in a Module of the Erythromycin Polyketide Synthase," BIOCHEMISTRY (1998) 37:2524-2528
	32.	Hallam *et al.*, "Nucleotide Sequence, Transcription and Deduced Function of a Gene Involved in Polyketide Antibiotic Synthesis in *Streptomyces coelicolor*," GENE (1988) 74:305-320
	33.	Hopwood *et al.*, "Product of 'Hybrid' Antibiotics by Genetic Engineering," NATURE (1985) 314(6012):642-644
	34.	Hopwood *et al.*, "Genes for Polyketide Secondary Metabolic Pathways in Microorganisms and Plants," Secondary Metabolites: Their Function and Evolution, Wiley Chichester (Ciba Foundation Symposium 171) (1992) 88-112
	35.	Hunaiti *et al.*, "Source of Methylmalonyl-Coenzyme A for Erythromycin Synthesis: Methylmalonyl-Coenzyme A Mutase from *Streptomyces erythreus*," ANTIMICROBIAL AGENTS AND CHEMOTHERAPY (1984) 25(2):173-178
	36.	Kao *et al.*, "Gain of Function Mutagenesis of the Erythromycin Polyketide Synthase. 2. Engineered Biosynthesis of an Eight-Membered Ring Tetraketide Lactone," J AM CHEM SOC (1997) 119(46):11339-11340
	37.	Kao *et al.*, "Manipulation of Macrolide Ring Size by Directed Mutagenesis of a Modular Polyketide Synthase," J AM CHEM SOC (1995) 117(35):9105-9106
	38.	Kao *et al.*, "Evidence for Two Catalytically Independent Clustersof Action Sites in a Functional Modular Polyketide Synthase," BIOCHEMISTRY (1996) 35(38):12363-12368
	39.	Kao *et al.*, "Engineered Biosynthesis of Structurally Diverse Tetraketides by a Trimodular Polyketide Synthase," J AM CHEM SOC (1996) 118(38):9184-9185
	40.	Kao *et al.*, "Engineered Biosynthesis of a Complete Macrolactone in a Heterologous Host," SCIENCE (1994)265:509-512
	41.	Khosla *et al.*, "Genetic Construction and Functional Analysis of Hybrid Polyketide Synthases Containing Heterologous Acyl Carrier Proteins," J BACTERIOL (1993) 175(8):2197-2204
	42.	Kramer *et al.*, "Rational Design and Engineered Biosynthesis of a Novel 18-Carbon Aromatic Polyketide," J AM CHEM SOC (1997) 119(4):635-639
V	43.	Kuhstoss *et al.*, "Production of a Novel Polyketide Through the Construction of a Hybrid Polyketide

EXAMINER:	DATE CONSIDERED: 11/26/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION	Docket Number 300622000212	Application Number 09/870,012
	Applicant: Chaitan KHOSLA et al.	
	Filing Date May 29, 2001	Group Art Unit 1652
(Use several sheets if necessary)	Mailing Date February 20, 2002	

OTHER DOCUMENTS *(Including author, title, Date, Pertinent Pages, Etc.)*

Examiner Initials	Ref. No.	Title
		Synthase," GENE (1996) 183:231-236
KK	44.	Lanz *et al.*, "The Role of Cysteines in Polyketide Synthase," J BIOL CHEM (1991) 266(15):9971-9976
	45.	Leadlay *et al.*, "The Erythromycin-Producing Polyketide Synthase," BIOCHEM SOC TRANSACTIONS (1993) 21:218-222
	46.	MacNeil *et al.*, "Complex Organization of the *Streptomyces avermitilis* Genes Encoding the Avermectin Polyketide Synthase," GENE (1992) 115:119-125
	47.	Malpartida *et al.*, "Molecular Cloning of the Whole Biosynthetic Pathway of a *Streptomyces* Antibiotic and its Expression in a Heterologous Host," NATURE (1984) 309:462-464
	48.	Malpartida *et al.*, "Physical and Genetic Characterisation of the Gene Cluster for the Antobiotic Actinorhodin in *Streptomyces coelicolor* A3(2)," MOL GEN GENET (1986) 205:66-73
	49.	Marsden *et al.*, "Stereospecific Acyl Transfers on the Erythromycin-Producing Polyketide Synthase," SCIENCE (1994) 263:378-380
	50.	McDaniel *et al.*, "Gain-of-Function Mutagenesis of a Modular Polyketide Synthase," J AM CHEM SOC (1997) 119(18):4309-4310
	51.	Oliynyk *et al.*, "A Hybrid Modular Polyketide Synthase Obtained by Domain Swapping," CHEM BIOL (1996) 3(10):833-839
	52.	Omura *et al.*, "Inhibition of the Biosynthesis of Leucomycin, A Macrolide Antibiotic, by Cerulenin," J BIOCHEM (1974) 75:193-195
	53.	Pereda *et al.*, "The Loading Domain of the Erythromycin Polyketide Synthase is not Essential for Erythromycin Biosynthesis in *Saccharopolyspora erythraea*," MICROBIOLOGY (1998) 144:543-553
	54.	Pieper *et al.*, "Remarkably Broad Substrate Specificity of a Modular Polyketide Synthase in a Cell-Free System," J AM CHEM SOC (1995) 117(45):11373-11374
	55.	Pieper *et al.*, "Cell-Free Synthesis of Polyketides by Recombinant Erythromycin Polyketide Synthesis," NATURE (1995) 378:263-266
	56.	Pieper *et al.*, "Purification and Characterization of Bimodular and Trimodular Derivatives of the Erythromycin Polyketide Synthase," BIOCHEMISTRY (1997) 36(7):1846-1851
	57.	Pieper *et al.*, "Erythromycin Biosynthesis: Kinetic Studies on a Fully Active Modular Polyketide Synthase Using Natural and Unnatural Substrates," BIOCHEMISTRY (1996) 35:2054-2060
	58.	Roberts *et al.*, "[^{3}H]Tetrahydrocerulenin, a Specific Reagent for Radio-Labelling Fatty Acid Synthases and Related Enzymes," FEBS LETT (1983) 159(1,2):13-16
✓	59.	Roberts *et al.*, "Use of [^{3}H]Tetrahydrocerulenin to Assay Condensing Enzyme Activity in

EXAMINER: KK DATE CONSIDERED: 11/20/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION	Docket Number 300622000212	Application Number 09/870,012
	Applicant: Chaitan KHOSLA et al.	
	Filing Date May 29, 2001	Group Art Unit 1652
(Use several sheets if necessary)	Mailing Date February 20, 2002	

OTHER DOCUMENTS *(including author, title, Date, Pertinent Pages, Etc.)*

Examiner Initials	Ref. No.	Title
		Streptomyces erythreus," BIOCHEM SOC TRANSACTIONS (1984) 12:642-643
KK	60.	Rudd *et al.*, "Genetics of Actinorhodin Biosynthesis by Streptomyces Coelicolor A3(2)," J GEN MICROBIOL (1979) 114:35-43
	61.	Shen *et al.*, "Enzymatic Synthesis of a Bacterial Polyketide from Acetyl and Malonyl Coenzyme A," SCIENCE (1993) 262:1535-1540
	62.	Sherman *et al.*, "Structure and Deduced Function of the Granaticin-Producing Polyketide Synthase Gene Cluster of *Streptomyces violaceoruber* Tü22," EMBO J (1989) 8(9):2717-2725
	63.	Sherman *et al.*, "Functional Replacement of Genes for Individual Polyketide Synthase Components in *Streptomyces coelicolor* A3(2) by Hetergenous Genes from a Different Polyketide Pathway," J BACTERIOL (1992) 174(19):6184-6190
	64.	Spencer *et al.*, "Purification and Properties of 6-Methylsalicylic Acid Synthase from *Penicillium patulum*, " BIOCHEM J (1992) 288:839-846
	65.	Wawszkiewicz *et al.*, "Propionyl-CoA Dependent $H^{14}CO_3$ -Exchange into Methylmalonyl-CoA in Extracts of Streptommyces erythraeus," BIOCHEMISCHE ZEITSCHRIFT (1964) 340:213-227
	66.	Wiesmann *et al.*, "Polyketide Synthesis *In Vitro* on a Modular Polyketide Synthase," CHEM BIOL (1995) 2(9):583-589

EXAMINER: Kathleen Kerr	DATE CONSIDERED: 11/20/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

#6
#9

Form PTO-1449

INFORMATION DISCLOSURE CITATION IN AN APPLICATION

Docket Number 300622000212	Application Number 09/870,012
Applicant: Chaitan KHOSLA et al.	
Filing Date May 29, 2001	Group Art Unit 1652
(Use several sheets if necessary)	Mailing Date August 21, 2002

U.S. PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Filing Date If Appropriate
KK	1.	09/1997	5,672,491	Khosla et al.	435	148	
	2.	03/1999	5,876,991	DeHoff et al.	435	183	
	3.	08/1999	5,945,320	Burgett et al.	435	183	

FOREIGN PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Country	Class	Subclass	Translation YES	Translation NO

OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title

EXAMINER: Kathleen Kerr

DATE CONSIDERED: 11/20/02

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.